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Structural correlates of prospective memory

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ABSTRACT

Prospective memory (PM) includes the encoding and maintenance of an intention, and the retrieval and execution of this intention at the proper moment in the future. The present study expands upon previous behavioral, electrophysiological, and functional work by examining the association between grey matter volume and PM. Estimates of grey matter volume in theoretically relevant regions of interest (prefrontal, parietal, and medial temporal) were obtained in conjunction with performance on two PM tasks in a sample of 39 cognitively normal and very mildly demented older adults. The first PM task, termed focal in the literature, is supported by spontaneous retrieval of the PM intention whereas the second, termed non-focal, relies on strategic monitoring processes for successful intention retrieval. A positive relationship was observed between medial temporal volume and accuracy on the focal PM task. An examination of medial temporal lobe subregions revealed that this relationship was strongest for the hippocampus, which is considered to support spontaneous memory retrieval. There were no significant structure–behavior associations for the non-focal PM task. These novel results confirm a relationship between behavior and underlying brain structure proposed by the multiprocess theory of PM, and extend findings on cognitive correlates of medial temporal lobe integrity.

1. Introduction

Prospective memory (PM) refers to the process of remembering to remember. PM requires the initial planning and formation of an intention, later recognition of a cue and recollection of its associated intention, and executing this intention in coordination with ongoing activity (Marsh, Hicks, & Watson, 2002). PM is fundamental to the performance of every-day tasks such as remembering to turn off one's cell phone in a movie theatre or remembering to stop for groceries on the way home from work. In typical event-based PM paradigms (i.e., responding to a specific event in the future), participants engage in a primary ongoing task while simultaneously remembering to make a unique response to infrequent targets associated with a previously encoded intention (McDaniel & Einstein, 2007).

According to the multiprocess theory (McDaniel & Einstein, 2000, 2007), qualitatively different processes support the retrieval of the PM intention depending upon the context. A determining factor is the degree to which encoded features of the PM cue are extracted as part of the ongoing activity (see Einstein et al., 2005; McDaniel & Einstein, 2007). For *non-focal* tasks, ongoing task processing does not stimulate processing of critical PM cue features (see Knight et al., 2011; McDaniel & Einstein, 2007). For example, when the PM cue is a particular syllable (e.g., "tor"), and the ongoing activity requires a category judgment (e.g., is "tornado" a member of given category "weather"), the ongoing task emphasizes semantic features, whereas the critical recognition features for the PM cue are syllabic. This lack of overlap requires additional strategic monitoring processes for successful non-focal PM cue recognition (Einstein et al., 2005; see Shallice & Burgess, 1991, and Smith, 2003 for views of PM monitoring).

For *focal* tasks, information relevant to the ongoing task overlaps with encoded PM cue features. In the just mentioned category-decision activity, the whole-word target "tornado" would be a focal cue, assuming people access semantic features during intention formation and when making category decisions. From the multiprocess theory perspective, such focal cues elicit spontaneous retrieval processes to support PM (see Einstein & McDaniel, 1996; McDaniel, Robinson-Riegler, & Einstein, 1998, for initial characterizations of spontaneous PM retrieval).

The predictions of the multiprocess theory were examined in a seminal study conducted by Einstein et al. (2005; see also Scullin, McDaniel, Shelton, & Lee, 2010) that manipulated cue focality. Participants demonstrated significant slowing when a non-focal PM demand was embedded in an ongoing task (relative to a control condition that involved only the ongoing task), but no such costs were observed when a focal PM demand was embedded. The ongoing task costs in the non-focal condition were directly associated

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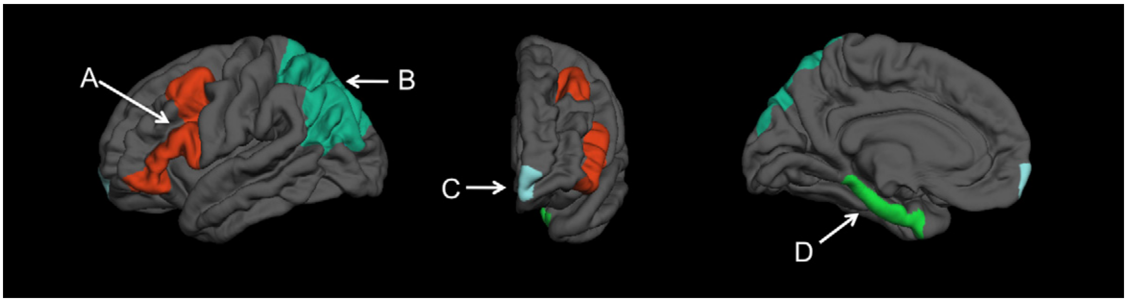

Fig. 1. Example of ROIs displayed on the template brain from Freesurfer. (A) Ventral/dorso-lateral prefrontal cortex; (B) lateral parietal cortex; (C) anterior prefrontal cortex; (D) medial temporal lobe.

with PM cue detection and declined over time during the task. The authors interpreted the ongoing task costs observed in the non-focal condition, and their decline over time, as evidence for an underlying, strategic monitoring process. The lack of ongoing task costs in the focal condition, accompanied by high PM performance, suggested a more reflexive, spontaneous retrieval process supporting PM without the need for an attention-demanding monitoring process. The critical point for the present study is that the multiprocess theory anticipates engagement of two brain networks, one tied to effortful modulations of attention, and another for spontaneous retrieval. Moreover, the relative importance of these networks to PM is dependent on the relative non-focal or focal nature of the task (McDaniel & Einstein, 2007, 2011).

An expanding interest in PM has encouraged investigation of its neural underpinnings (e.g., Burgess, Gonen-Yaacovi, & Volle, 2011; Martin et al., 2007; McDaniel & Einstein, 2011; West, 2011). Using PET and fMRI, researchers have found consistent activation of several brain regions when examining event-related PM; most prominent among these is an anterior prefrontal region located approximately in Brodmann area 10 (BA 10; Burgess, Quayle, & Frith, 2001, 2011; Reynolds, West, & Braver, 2009). As the vast majority of this work utilizes non-focal tasks, this region is likely an integral node in the network supporting effortful attentional processes needed for non-focal PM (Simons, Scholvinck, Gilbert, Frith, & Burgess, 2006). Although much focus has been on anterior prefrontal cortex, PM success has also been linked to parietal (Burgess et al., 2011, 2001; Martin et al., 2007; Reynolds et al., 2009), and medial temporal lobe (MTL, see Burgess, Maguire, & O'Keefe, 2002 for a review) regions. Additionally, as a mainstay of cognitive control, the lateral parietal and dorsolateral prefrontal regions of the dorsal attentional network (Corbetta & Shulman, 2002) are other potential loci facilitating non-focal performance.

For a network supporting spontaneous retrieval of PM intentions, there is a strong basis to examine the MTL. Functional activations in the hippocampus are tied to spatial, episodic, and recognition memory (Burgess et al., 2002; Eichenbaum, Yonelinas, & Ranganath, 2007), and even focal PM performance in a naturalistic setting (Kalpouzos, Eriksson, Sjolie, Molin, & Nyberg, 2010). Similarly, the volumes of MTL structures, in particular the hippocampus, have been linked to episodic (e.g., Head, Rodrigue, Kennedy, & Raz, 2008) and spatial memory (e.g., Erickson et al., 2009). The importance of the hippocampus for relational memory (Eichenbaum & Cohen, 2001; Konkel & Cohen, 2009) along with its automaticity of function (Konkel & Cohen, 2009; Moscovitch, 1994), suggest that it may be crucial for the demands of a focal PM task (see McDaniel & Einstein, 2007; McDaniel et al., 1999). Although the hippocampus has a strong role in recollection, its surrounding structures may be integral for different aspects of memory (Aggleton & Brown, 2006; Ranganath et al., 2004). As such, the MTL subregions may be differentially important for PM.

The behavioral and functional studies to date suggest several mechanisms and brain regions important for successful performance of PM. To the authors' knowledge, only studies of neurological patients (e.g., Groot, Wilson, Evans, & Watson, 2002; Mathias & Mansfield, 2005) have looked at the link between brain structure and performance on PM tasks, and no studies have examined how these relationships differ depending on type of PM task (i.e., non-focal vs. focal). Here we examine relationships between focal and non-focal PM performance and grey matter volume in four regions-of-interest (ROIs) in a convenience sample of cognitively normal and very mildly demented older adults. We predicted that focal performance would be selectively associated with the MTL, with the strongest relationship with the hippocampus proper, whereas prefrontal and parietal region volumes would be especially associated with non-focal performance.

2. Materials and methods

2.1. Participants

Participants were a subsample of community-dwelling older adults from a larger study examining PM performance, aging and dementia (McDaniel et al., 2011). Participants were recruited from the Knight Alzheimer's Disease Research Center at Washington University and screened for neurological illness (e.g., Parkinson's, Huntington's, seizures, major head injury). Participants were classified as cognitively normal (CDR = 0; $n = 21$ (16 female)) or very mildly demented (CDR = 0.5; $n = 18$ (12 female)) based on the Clinical Dementia Rating scale (CDR; Morris, 1993). A health composite score was created based on the absence or presence (coded 0 or 1) of hypertension, diabetes, history of heart problems (i.e., atrial fibrillation, angioplasty, bypass surgery, congestive heart failure, or pacemaker implantation), history of stroke or transient ischemic attack, history of depression, and mild head injury. The resulting value between 0 and 6 captures multiple health factors into a general measure of overall health, while reducing the need for multiple covariates (reducing power) in the relatively small sample. Demographics characterizing the sample are presented in Table 1.

2.2. Behavioral task

Participants were engaged in an ongoing category-judgment task where they decided whether an exemplar word was a member of a specified category (e.g., green COLOR; see Einstein et al., 2005). The exemplar word was always presented in lowercase letters on the left, and the category was always simultaneously displayed in uppercase letters on the right. Three counterbalanced blocks of 106 word-category pairings were presented, with a category match on half of the trials. Two of these blocks had an additional embedded PM task; the third was a control block with only the ongoing category judgment task. For the focal PM block, participants were instructed to press "Q" whenever they saw a particular word (either "tortoise", "raspberry", or "aluminum"). For the non-focal PM block, participants were instructed to press "Q" if they ever saw a word containing a particular syllable (either 'tor', 'ras', or 'min'). The PM targets always occurred in the exemplar rather than the category word and the PM targets always appeared on trials 31, 72, and 102 of both the focal and non-focal blocks. For each PM block, the PM cue was presented three times, increasing total trials in these blocks to 109 trials. The low number of PM trials is intended to maintain the design as a true PM task rather than creating a vigilance task, and as such, is intended to capture PM processes similar to everyday life. Because the same PM target word was repeated three times in the focal condition, non-target words were also repeated to remove any distinctiveness that might arise from this repetition (cf. McDaniel & Einstein, 1993). Eleven non-targets were